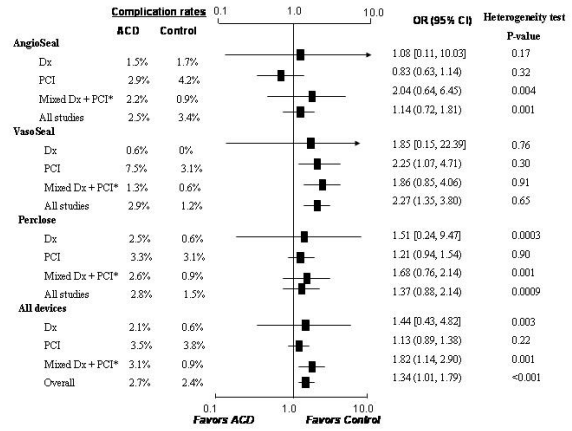


*Mixed Dx+PCI: publications where the data were provided without separation to Dx and PCI.

3:00 p.m.

818-5 **Percutaneous Transfemoral Coronary and Peripheral Procedures via Aortofemoral Synthetic Vascular Grafts: A Review of 123 Diagnostic and Interventional Cases**

Michael J. Gallagher, Simon R. Dixon, Mohan C. Madala, Renny Abraham, Steven D. Rimar, William W. O'Neill, Joel K. Kahn, William Beaumont Hospital, Royal Oak, MI

Background: Few data exist regarding the incidence of vascular complications associated with transfemoral catheterization and sheath placement into synthetic vascular grafts.
Methods: We performed a retrospective analysis of all patients who underwent aortofemoral bypass surgery at our institution between January, 1991 and July, 2003. Those patients who underwent subsequent transfemoral catheterization were selected. A total of 123 procedures were performed in 70 patients between February, 1994 and April, 2003.
Results: One hundred and thirteen coronary (91.9%) and 10 peripheral (8.1%) procedures were performed, including sixty-four (52.0%) interventional (angioplasty and/or stent), and 59 (48%) diagnostic procedures. Two of the interventional procedures included placement of an intraaortic balloon pump via the graft. The interval between graft implantation and sheath placement was 2.9 ± 2.1 years (range 4 days to 10.3 years). Four procedures (3.3%) required concomitant brachial or radial access due to inability to access the ascending aorta via the femoral approach. Pre-procedural anticoagulation included aspirin (91.9%), clopidogrel (28.5%), warfarin (10.6%), and intravenous heparin (39.0%). The peak activated clotting time was 313 ± 89 seconds. The procedure time was 53.2 ± 34.1 minutes, and sheaths were pulled an average of 5.2 hours after catheterization. Adverse events related to vascular access occurred in 8/123 (6.5%) procedures. Complications included blood transfusion (4.1%), thrombotic occlusion (1.6%), and retroperitoneal bleed (0.8%). The two cases of thrombotic occlusion were associated with early clinical signs of diminished perfusion. One patient required surgical thrombectomy and the other was treated with intraarterial local thrombolysis. There were no cases of graft infection or pseudoaneurysm formation, nor any deaths attributable to vascular access complications.
Conclusion: Transfemoral sheath entry into a synthetic aortofemoral bypass graft is associated with a low incidence of adverse vascular events. However, careful observation and follow up during the 24-hour post catheterization period is critical.

3:15 p.m.

818-6 **Women Remain at Higher Risk for Retroperitoneal Hematoma After Percutaneous Coronary Intervention in the Era of Glycoprotein IIb/IIIa Inhibitors and Vascular Closure Devices**

H M Omar Farouque, Jennifer A. Tremmel, Meenakshi Aggarwal, Farshad Raissi Shabari, William F. Fearon, Mehrdad Rezaee, Alan C. Yeung, David P. Lee, Stanford University Medical Center, Stanford, CA

Background: The incidence, clinical features, and determinants of retroperitoneal hematoma (RPH) after percutaneous coronary intervention (PCI) have been previously described. We examined these variables in the current era of widespread glycoprotein (GP) IIb/IIIa inhibitors and vascular closure devices (VCDs).
Methods: 3,230 PCI procedures were performed from January 2000 to August 2003. There were 22 cases of radiographically documented RPH. Cases were compared to a random sample of 50 controls using chi-square and logistic regression.
Results: The incidence of RPH was 6.8/1000 cases. Mean age±SD was 67±12 years in both groups. Cases and controls did not differ in prevalence of hypertension, diabetes, or hyperlipidemia. Median time from procedure end to onset of clinical signs was 126 minutes (range 15-840). Symptoms included lower abdominal pain (59%), diaphoresis (59%), groin pain (45%), and back pain (18%). Groin hematoma was evident in 32%. Hypotension occurred in 91%, with a mean BP nadir of 78/40 mmHg. Bradycardia requiring atropine occurred in 36%. Hematocrit dropped from 37.5±3.4% to 27.1±3.8% (p=0.007). All cases had blood loss anemia and at least two of the above clinical features. Mean hospital stay was longer in RPH cases (2.2±1.3 *vs.* 1.7±1.5 days, p=0.06). The use of GP IIb/IIIa inhibitors and the method of vascular closure had no effect on the risk of RPH. There was also no association between RPH and acuity of PCI (elective *vs.* emergent), duration of procedure, heparin dose, ACT level, arterial sheath size, insertion of a venous sheath, or prior femoral artery puncture. Female sex was most strongly associated with RPH (OR 5.0, 95% CI 1.7-14.5). Angiographic analysis revealed that a higher femoral artery puncture in relation to the femoral head (superior third of the femoral head and higher *vs.* mid third and lower) was also associated with RPH (OR 4.2, 95% CI 1.3-14.0).
Conclusion: With the widespread use of GP IIb/IIIa inhibitors and VCDs, being a woman remains a significant risk factor for RPH, as does a more superior femoral artery puncture. Awareness of the determinants and clinical features of RPH may aid in prevention, early recognition, and prompt treatment.

POSTER SESSION

1100

Percutaneous Intervention: Pharmacologic and Biologic Adjuncts

Monday, March 08, 2004, 3:00 p.m.-5:00 p.m.
Morial Convention Center, Hall G
Presentation Hour: 3:00 p.m.-4:00 p.m.

1100-55 **Intravenous Mesenchymal Stem Cell Therapy Early After Reperfused Acute Myocardial Infarction Improves Left Ventricular Function and Alters Ventricular Electrophysiologic Properties**

Matthew J. Price, Chung-Chuan Chou, Malka Frantzen, Takashi Miyamoto, Saibal Kar, Dougal McClean, Suzhen Guo, Steve Lee, Prediman K. Shah, Bradley J. Martin, Michael Lill, James S. Forrester, Peng-Sheng Chen, Raj R. Makkar, Cedars Sinai Medical Center, Los Angeles, CA

Background: Direct intramyocardial injection of stem cells improves LV function. However, the injection of immature cells has been associated with an increased risk of ventricular arrhythmia. We hypothesized that the IV infusion of allogeneic mesenchymal stem cells (MSCs) without immunosuppresion after acute MI would improve LV function but might be accompanied by pro-arrhythmic electrical remodeling.
Methods: An apical MI was induced in swine by balloon occlusion-reperfusion of the mid-LAD. Animals received either no treatment, or, 30 minutes after reperfusion, DiI-labeled allogeneic bone marrow derived MSCs ($3.2\pm0.4 \times 10^8$ cells) were infused IV. LV function was evaluated by LV cineangiography and wall thickness by echocardiography. Epicardial effective refractory periods (ERPs) were determined at 3 month sacrifice. Spectral imaging by confocal microscopy was used to identify Di-I in tissue specimens.
Results: At 3 months, MSC treated pigs [n=7] had significantly higher LVEF than controls [n=8] (50±1% vs 44±1%, p=0.015), as well as significantly higher LV systolic pressure (144±5 mmHg vs. 119±5 mmHg, p=0.01). The mean increase in LVEDV over time tended to be greater in the control group ($48\pm6cm^3$ vs.$32\pm6cm^3$, p=0.09). The wall thickness of normal, non-infarcted myocardium increased significantly more in controls than in treated animals. ERPs of the MSC group were significantly shorter than controls at all pacing cycle lengths in LV peri-infarct, LV free wall (FW), and right ventricular (RV) FW (225±6, 227±5, 225±6 ms, vs 251±6, 251±6, 247±7 ms, all p<=0.002). The mean slope of the ERP restitution curves was steeper in the MSC group than in controls (1.6±0.8 vs 1.0±0.4, p=0.02). DiI was identified in the lungs and myocardium of treated animals.
Conclusions: IV infusion of MSCs soon after reperfused acute MI in swine improves LV function, lessens compensatory hypertrophy of non-infarcted myocardium, shortens ERP, and steepens the ERP restitution curve. Clinical trials assessing the efficacy of IV MSC therapy after MI in humans should include arrhythmia monitoring.

1100-56 **Comparison Between Intracoronary Infusion and Direct Transendocardial Injection of Mesenchymal Stem Cells in a Dog Acute Ischemia Model**

Emerson C. Perin, Joao A. Assad, Guilherme V. Silva, Stephanie Coulter, Judy Ober, Jing Lin, Andre L. Sousa, Silvio Litowski, Yong Geng, Bradley J. Martin, William K. Vaughn, James T. Willerson, Texas Heart Institute, Houston, TX

Background: Experimental data suggest that mesencymal stem cell (MSC) therapy contributes to healing after acute myocardial infarction(AMI). The ideal route of administration is still contrversial.
Methods: A total of 10 dogs were divided in three groups:a)Control n=3; b)Intracoronary (IC) n=3 and c) NOGA guided transendocardial injections (TEI) n=4. All animals had an anterior wall AMI induced by ligation of LAD artery for three hours and then reperfused. The animals received cell therapy (100 million MSC's(Osiris)) 1 wk after AMI and were sacrificed 2 wks after cell therapy. 2D-echo was performed immediately before AMI, cell therapy and sacrifice. NOGA mapping was performed immediately before cell therapy and sacrifice. Ischemic area was measured by NOGA. ANOVA was performed.
Results: The 2D-echo findings concerning ejection fraction (EF), end-diastolic dimension (EDD), end-systolic dimension (ESD), and ischemic area are presented in table 1. The TEI group had a statistically significant increase in EF (p=0.006), a reduction in EDD(p=0.04), a reduction in ESD (p=0.02), and more importantly a reduction in ischemic area (p=0.006) when compared to the control group. All the other comparisons did not reach statistical significance (p>0.05).

Conclusion: There were no complications associated with TEI after AMI. This preliminary data with a small number of animals suggests that NOGA guided TEI may be superior to IC delivery. Thus, direct delivery of MSC's may play an important role even after an AMI .

	Control	TEI	IC

	pre-cells	post-cells	pre-cells	post-cells	pre-cells	post-cells
EDD(mm)	4.2±0.1	3.97±0.19	3.9±0.3	3.55±0.15	4.0±0.08	3.93±0.26
ESD(mm)	3.47±0.04	3.17±0.2	3.1±0.3	2.65±0.33	3.1±0.25	3±0.21
EF(%)	32±1.41	34±2.9	33±3.2	49±9	34±2.1	41±4.3
Ischemic Area(%LV)	19.8±4	20.4±8	37.9±9.8	6.8±5.3	25.8±11.7	6±4.3

1100-57

Catheter-Based Transplantation of Autologous Bone Marrow Mononuclear Cells Safely Improves Collateral and Capillary Network in Adult Swine With Myocardial Ischemia

Aysegul Yegin, Mio Ebato, Fernando Tondato, Bunken Ebato, Jianhua Cui, Traci Goodchild, Stephen C. Frohwein, Jesse Rios, James F. Sanzo, Keith Robinson, Mark Ungs, Nicolas A. Chronos, American Cardiovascular Research Institute, Atlanta, GA

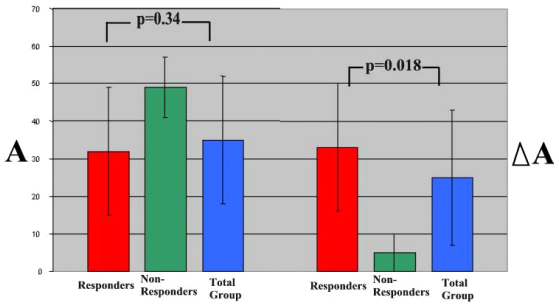
Background: To date, it is unclear whether intramyocardial transplantation of autologous bone marrow derived mononuclear cells (BM-MNCs) enhances neovascularization in adult myocardium. We tested the hypothesis that catheter-based delivery of BM-MNCs augments neovascularization in an adult porcine model of chronic ischemia. Methods: Ameroid constrictor was implanted around proximal left circumflex coronary artery (LCX) in adult Yucatan swine. Animals with LCX occlusion of < 90% were excluded from the study. At 4 weeks, pigs were randomized to receive freshly isolated BM-MNCs (n=8) or culture medium (DMEM) as control (n=8). Under general anesthesia, bone marrow (30-50 ml) was aspirated from sternum and if necessary, iliac crest. Mononuclear cells were isolated using density-gradient centrifugation method (Histopaque 1077). A total of 1 x 10^8 cells were injected at 10 sites (5 in the ischemic, and 5 in the non-ischemic region) using Boston Scientific Stiletto™ catheter with intracardiac echocardiography (ICE) guidance. Baseline (4 wk) and follow-up (8 wk) evaluations included coronary angiography (Rentrop score), dobutamine stress echocardiography, and myocardial blood flow by microspheres. Tracking of BM-MNCs was performed in additional pigs (n=3). Tissue samples were stained with PKH-26 to verify cell viability and DAPI (diamino-phenylindole) for intact nuclear DNA, 2 and 4 weeks after delivery. Results: Collateral (Rentrop) Scores: Left-to-left collaterals significantly improved in the BM-MNC treated group (p=0.031). Cell tracking study: Ischemic areas contained higher amount of PKH-26 positive cells co-localizing with DAPI, compared to non-ischemic regions. Transplanted BM-MNCs clustered in areas without abundant cellular structure. A significant increase was found in total capillary area in the LCX (ischemic) region in endocardial (p=0.016) and epicardial (p=0.044) sections in BM-MNC treated pigs compared to the control group. Conclusion: Catheter-based intramyocardial transplantation of autologous BM-MNCs safely enhances collateral and capillary network in adult swine with chronic myocardial ischemia.

1100-58

Interpretation of the Actual Platelet Inhibition Induced by Clopidogrel: A New Look at How to Represent Drug Response

Paul A. Gurbel, Waiel M. Samara, Kevin P. Bliden, Sinai Center for Thrombosis Research, Baltimore, MD

Background: Mean pre- and post- treatment % platelet aggregation is commonly used to describe clopidogrel- induced inhibition and may miss non-responders. **Methods:** Individual responses to clopidogrel were studied by 5 µM ADP aggregation (A) in pts (n = 68) pre and at 5 days post-stenting. All pts received aspirin 325mg ; 300 mg clopidogrel at the time of stenting ; and 75mg qd . A was recorded as the maximum % change in light transmittance from baseline. Individual responses were measured at 5 days as the absolute change in aggregation (Δ A) from pre-to post-treatment. (Δ A= pre-treatment A minus post-treatment A ; non-response = Δ A <10%.
Results: Pre-treatment A was 60 ± 17 and fell to 35 ± 17 after clopidogrel (p<.0001, 42% relative inhibition) and 16/68 patients (24%) were non-responders (figure). Non-responders had higher platelet reactivity (p=.0002). However, total group A was not significantly different from the group of responders (p = .34). By reporting the data as ΔA the presence of non- responders in unmasked (figure).
Conclusion: Non-responders are entirely unrecognized by the current practice of reporting mean aggregation data that overestimates the actual drug effect in certain patients. Clinicians should be aware of non-response and its potential effect on outcomes. We recommend a more accurate approach to estimate the drug's effect would be to account for those patients who are non-responsive by reporting the individual change in aggregation from pre-treatment to post-treatment.



1100-59

High-Dose Clopidogrel Loading Rapidly Reduces Both Platelet Inflammatory Marker Expression and Aggregation

Frank J. Zidar, David J. Moliterno, Deepak L. Bhatt, Kandice Kottke-Marchant, Marelene Goormastic, Edward F. Plow, Eric J. Topol, Cleveland Clinic, Cleveland, OH

Background: Pretreatment with the platelet antagonist clopidogrel has been shown to reduce short and long-term ischemic events after percutaneous coronary intervention. The optimal clopidogrel loading dose and the timing of its benefit remain unclear. Moreover, it is uncertain whether these benefits are from inhibition of platelet-mediated aggregation, inflammation, or both. We sought to determine the response to a 300mg clopidogrel loading versus a 600mg (high dose) loading on the time-course of aggregation and inflammation suppression.
Methods: 12 healthy volunteers were given 300mg of clopidogrel, and blood samples were obtained at baseline and 2, 4, and 6 hours. After a 2-week washout period, these subjects were given 600mg of clopidogrel and serial blood sampling was repeated. Platelet aggregation was quantified using turbidimetric aggregometry with ADP (20uM) as the agonist, and results were evaluated as percent inhibition of baseline aggregation. Platelet CD40L and P-selectin expression in ADP-activated samples were quantified by flow cytometry, and results were evaluated as percent positive cells.
Results: Complete data were available on 10 subjects, 50% men with a mean of 35 years (+/- 7 SD).

	Dose (mg)	**Time (hours) : Mean**			
		0	**2**	**4**	**6**
% Inhibition from baseline aggregation	300	0	34.6	32.7	33.5
	600	0	48.2*	43.9*	50.9*

Difference between 300 and 600 at 0 (p=NS), 2 **(p=0.009)**, 4 **(p=0.02)**, 6 **(p=0.0008)**

CD40L % positive cells	300	27.0	21.4	13.7	18.6
	600	24.0	16.0	11.6	9.8*

Difference between 300 and 600 at 0, 2 and 4 hours (p=NS); 6 hours **(p=0.01)**

P-selectin % positive cells	300	88.6	84.1	82.4	81.9
	600	81.1	75.7	72.3*	67.1*

Difference between 300 and 600 at 0 and 2 (p=NS), 4 hours **(p=0.02)**, 6 hours **(p=0.05)**

Conclusion: Beyond a greater early inhibition of platelet aggregation, a high loading dose of clopidogrel rapidly and more effectively suppresses platelet inflammatory markers. These anti-inflammatory effects likely play a key role in the clinical benefit from clopidogrel pretreatment.